ORIGINAL REPORT

Red cell antigen prevalence predicted by molecular testing in ethnic groups of South Texas blood donors

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Alloimmunization to red blood cell antigens is seen in patients receiving chronic blood transfusion. Knowing the prevalence of blood group antigens of the different ethnicities of South Texas donors can provide better management of rare blood inventory for patients in this geographical area. A total of 4369 blood donors were tested and analyzed for various antigens in the following blood group systems: ABO, Rh, Kell, Duffy, Kidd, MNS, Lutheran, Dombrock, Landsteiner-Wiener, Diego, Colton, and Scianna. Donors tested to be group O or A were serologically tested for the Rh (C, E, c, e) antigens. Those that tested as presumably R_1R_1, R_2R_2, or R_0r were then genotyped. Donors constituted three major ethnicities: black (18.3%), Hispanic (36.3%), and Caucasian (41.1%); ethnicities comprised of Asian, American Indian, multiracial, and other accounted for the remaining donors (4.3%). The most likely common Rh phenotype for each ethnicity is as follows: black $-R_0r$ (44.4%), Hispanic $-R_1R_1$ (59.0%), and Caucasian $-R_1R_1$ (38.9%). The prevalence of Kell, Duffy, and Kidd blood group system antigens in black and Caucasian donors is comparable with published reports for the entire U.S. The black South Texas donor population had an 8.8 percent increase in prevalence of the Fy(a+b–) phenotype as compared with these published reports; the Hispanic South Texas donor population had a prevalence of 36.1 percent of the Fy(a+b–) phenotype. Regarding the Diego blood group system, the Hispanic donor population in South Texas had a prevalence of 93.5 percent for the Di(a–b+) phenotype as compared with published reports for the entire U.S. (>99.9%). The Hispanic population had a prevalence of 7.9 percent of donors testing as M–N+S–s+ as compared with 20.2 percent and 15.6 percent for black and Caucasian donors, respectively. This study helped us determine the prevalence of each of the blood group antigens in the South Texas donor population to establish and maintain adequate rare inventory of each. Molecular red blood cell genotyping allows transfusion services to increase their availability of rare phenotypes for chronically transfused patients. ***Immunohematology* 2015;31:166–173.**

Key Words: blood group antigens, alloimmunization, ethnicity, molecular genotyping, blood group system

Donating blood and blood components can potentially save a recipient's life. Red blood cell (RBC) transfusion can also cause alloimmunization, which can lead to shortened RBC survival and/or transfusion reactions.[1] In the laboratory blood bank, routine pretransfusion testing is performed on patient samples to mitigate possible immune-mediated hemolytic transfusion reactions (HTRs) by observing antigen–antibody reactions in vitro before blood is released for transfusion.[2] Despite these procedures, there have been instances when a patient has had a transfusion reaction due to the development of red blood cell antibodies in the Rh, Kidd, Duffy, Kell, and MNS blood group systems.[3] Delayed hemolytic transfusion reactions (DHTRs) can occur, causing fever and anemia, days or weeks after a blood transfusion.[3] The risk of RBC alloimmunization increases as the number of transfusions increase.[4] The probability of developing additional antibodies to RBC antigens increases for those who have developed alloantibodies, especially in non-hemato-oncologic patients.[4] Because of their hemoglobinopathy, patients with sickle cell disease (SCD) may be chronically transfused and are at higher risk of developing RBC alloantibodies.[5] Presently, many facilities antigen-match their patients with SCD for Rh (C, E, c, e) and Kell (K) to prevent RBC alloimmunization. Extended matching for Duffy (Fy^a, Fy^b), Kidd (Jk^a, Jk^b), and MNS (M, N, S, s) is rarely performed by facilities.[6]

The probability of finding specific blood phenotypes depends on the prevalence of that phenotype in a population.[7] The purpose of this study was to determine the prevalence of various RBC antigens in the blood donor population of South Texas. By doing so, an adequate phenotyped blood supply can be established and maintained to help manage the needs of chronically transfused patients, such as patients with SCD.

Material and Methods

The institutional review board of The George Washington University (Washington, DC) and the research committee from BioBridge Global (San Antonio, TX) gave approval to retrieve pertinent data from volunteer allogeneic blood donors collected by the South Texas Blood & Tissue Center (STBTC), San Antonio, TX; STBTC collects about 150,000 blood units a year and supplies blood products to 67 hospitals in 43 South Texas counties. For this study, records from 4369 donors from the period of June 2007 to November 2014 were analyzed.

Random donors were selected at least once a week from different blood donor drives in the South Texas area. Each of these drives had between 75 to 100 possible whole blood donations. Donor samples received all required routine donor testing (namely, serological testing to determine ABO and D, and unexpected antibodies) and viral marker testing for infectious diseases. Informed consent for laboratory testing was received at donor registration using the donor history questionnaire form. An existing ethylenediaminetetraacetic acid (EDTA) blood sample tube collected at the time of donation was retrieved for this testing.

These donor samples were tested on the Beckman Coulter PK7300 analyzer (Olympus, Center Valley, PA) for ABO and D, C (RH2), E (RH3), c (RH4), and e (RH5). Group O and A donor samples that serologically tested as D+C+E−c−e+ [probable R_1R_1 (DCe/DCe)], D+C−E+c+e− [probable R_2R_2 (DcE/DcE)], or D+C−E−c+e+ [probable R_0r (Dce/ce)] with the PK7300 were retrieved for molecular testing. In addition, donors were randomly selected for molecular testing if they met one of three criteria: at least 10 or more blood donations in their history, self-designated as black, or D−.

The DNA for the molecular test was extracted from the donor sample using the fully automated QIAcube (QIAGEN, Valencia, CA). The BioArray HEA BeadChip (HEA 1.1) system (Immucor, Norcross, GA) was used from June 2007 to February 2009 to genotype each selected donor sample for multiple human erythrocyte antigens by DNA analysis. The BioArray HEA BeadChip (HEA 1.2) system was used for testing from March 2009 to November 2014. Genotyping for RBC antigens included those in the Rh (C, E, c, e, V, VS), Kell (K, k), Duffy (Fy^a, Fy^b), Kidd (Jk^a, Jk^b), MNS (M, N, S, s), Lutheran (Lu^a, Lu^b), Dombrock (Do^a, Do^b, Hy, Jo^a), Landsteiner-Wiener (LW^a, LW^b), Diego (Di^a, Di^b), Colton (Co^a, Co^b), and Scianna (Sc1, Sc2) blood group systems. The HEA 1.2 version included Kp^a, Kp^b, Js^a, and Js^b antigens of the Kell system.

The PK7300, BioArray, and QIAcube systems were used in accordance with manufacturer's instructions and standard operating procedures.

Statistical Analysis

The prevalence of blood types, ethnicities, donor age, and the various RBC phenotypes were calculated using SPSS Statistics, version 22.0 (IBM Corporation, Armonk, NY). Genotype occurrence, antigen-negative phenotype calculations, and phenotype prevalence were determined. The Hardy–Weinberg equilibrium formula was used to calculate genotype occurrence. Antigen-negative phenotype was calculated by multiplying the negative prevalence values for particular antigens. Phenotype prevalence was calculated as a percent, given the total positive results divided by the total tested of each antigen in the blood group systems.

Results

Data from 4369 South Texas whole blood donors were analyzed in this study. The ethnicity, age, and gender percentages were calculated based on information from the donation records. Thirty-one donors did not indicate their ethnicity, leaving a total of 4338 donors studied. The percentage for those donors who indicated their ethnicity is as follows: 18.3 percent black, 0.2 percent American Indian (AIAN), 1.3 percent Asian/Pacific Islander (ASPI), 41.1 percent Caucasian (CAUC), 36.3 percent Hispanic (HISP), 1.6 percent multiracial (MULT), and 0.6 percent other (OTHR; unable to determine proper ethnicity due to limitations of computer system ethnicity choices).

The mean age of the donors in this study was 42.7 years, and the most frequent age was 21 years. The youngest donor was 16 years old and the oldest donor was 91 years old. The gender distribution of each ethnicity was the following (% female/% male): black (50.1/49.9), AIAN (44.4/55.6), ASPI (46.4/53.6), CAUC (43.8/56.2), HISP (51.7/48.3), MULT (52.2/47.8), and OTHR (42.9/57.1).

Donors with blood groups A and O were specifically selected for this study because these blood groups occur most frequently in CAUC (43%, 44%) and black (27%, 49%) populations, respectively.[8] In addition, group O individuals are considered universal donors, since their RBCs are ABO-compatible with the plasma of group O, A, B, and AB recipients.[2] Therefore, the donors for this study were not random, but selected; 75.1 percent had blood group O, and 18.9 percent had blood group A, as shown in Table 1. In addition, blood group B and AB donors were 5.4 percent and 0.6 percent, respectively. The prevalence of D (RH1) in these donors was 86.6 percent, as shown in Table 1. These blood group percentages are consistent with the algorithm used in this study for retrieving samples for genetic testing. There were four ethnicities (AIAN, ASPI, MULT, and OTHR) that were not included for further analysis in the study, because the percentages of these ethnicities were all less than 2.0 percent of the total.

Table 2 summarizes the comparison of published percentages of black and CAUC phenotypes with those of South Texas donors who are black, CAUC, and HISP.[8] Donor samples that typed as presumably R_1R_1, R_2R_2, and R_0r were specifically retrieved for this study; these types are negative for at least

Table 1. Prevalence of ABO group and D type in South Texas donors by ethnicity*

	Prevalence (%)							
Blood group/D type	Black	AIAN	ASPI	CAUC	HISP	MULT	OTHR	Total
O	65.4	88.9	61.8	72.6	83.6	69.1	71.4	75.1
A	22.6	11.1	21.8	22.7	12.4	26.5	21.4	18.9
B	10.8	0.0	0.0	4.0	3.9	2.9	7.1	5.4
AB	1.3	0.0	0.0	0.7	0.1	1.5	0	0.6
D	95.9	66.7	100	76.9	92.5	89.7	78.6	86.6

*N = 4338; AIAN = American Indian; ASPI = Asian/Pacific Island; CAUC = Caucasian; HISP = Hispanic; MULT = Multiracial; OTHR = Other.

two antigens in the Rh blood group system (C, E, c, e). In the black population, the prevalence was 4.0 percent for R_1R_1 and 1.7 percent for R_2R_2 as compared with published phenotype prevalence for this ethnicity of 2.0 percent and 0.2 percent, respectively. The CAUC population prevalence for R_1R_1 was 38.9 percent and for R_2R_2 was 6.1 percent, as compared with published phenotype prevalence for this ethnicity of 18.5 percent and 2.3 percent, respectively. The HISP population had one of the highest phenotype prevalences observed for R_1R_1 at 59.1 percent and for R_2R_2 at 18.5 percent, as compared with the prevalence of published black and CAUC phenotypes. Because donor samples with known R_1R_2 phenotypes were not pulled for this study, there was a decrease in these phenotypes for black (3.1%) and CAUC (4.3%) populations as compared with published reports of 4.0 percent and 13.3 percent, respectively. The HISP donor population had a prevalence of 2.0 percent for the R_1R_2 phenotype.

The prevalence for the phenotype rr (D−C−E−c+e+) was observed as the highest within the CAUC population (21.9%), followed by the HISP (6.8%) population and finally the black population (3.5%), as compared with those published reports of black (6.8%) and CAUC (15.1%) populations. The prevalence of these selected phenotypes was higher than the published phenotype prevalence, due to retrieval of these phenotypes for this study. The phenotype prevalence of R_1r for the CAUC population was 19.9 percent, as compared with published reports of 34.9 percent. It is lower in this study because this phenotype knowingly was not retrieved for genotyping.

Table 3 summarizes the prevalence of Kell, Duffy, and Kidd phenotypes of South Texas donors who were black, CAUC, and HISP, as compared with published black and Caucasian reports.[8] The black population results were comparable with the published phenotypes, with the exception of an increase in Kp(a+b+), Fy(a+b−), and Fy(a+b+) phenotypes. The South Texas donor prevalence for these phenotypes was 2.3 percent, 17.8 percent, and 4.5 percent, respectively, as compared with published reports of rare, 9 percent, and 1 percent, respectively. In addition, a decrease in prevalence was seen with Fy(a−b−)

Table 2. Rh blood group phenotype prevalence: comparison of South Texas donors with published reports[8]

Phenotype	Black prevalence (%)		CAUC prevalence (%)		HISP prevalence (%)
Wiener	N = 747*	Published reports	N = 1785*	Published reports	N = 1570*
R_1R_1	4.0	2.0	38.9	18.5	59.0
R_2R_2	1.7	0.2	6.1	2.3	18.5
R_1r	26.0	21.0	19.9	34.9	7.6
R_2r	17.0	18.6	7.5	11.8	2.6
R_0r	44.4	45.8	1.3	2.1	2.4
R_zR_z	0.0	RARE	0.0	0.0	0.1
R_1R_z	0.1	RARE	0.1	0.2	0.6
R_1R_2	3.1	4.0	4.3	13.3	2.0
r′r	0.0	RARE	0.1	0.8	0.0
r′r′	0.0	RARE	0.1	RARE	0.1
r″r	0.1	RARE	0.1	0.9	0.2
rr	3.5	6.8	21.9	15.1	6.8
r′r″	0.0	RARE	0.0	0.1	0.1

*South Texas donors.
CAUC = Caucasian; HISP = Hispanic.

Table 3. Prevalence of Kell, Duffy, and Kidd blood group phenotypes: comparison of South Texas donors with published reports[8]

		Black			CAUC			HISP	
		South Texas donors		Published reports	South Texas donors		Published reports	South Texas donors	
Blood group system	Phenotype	*N*	Prevalence (%)	Prevalence (%)	*N*	Prevalence (%)	Prevalence (%)	*N*	Prevalence (%)
Kell	K–k+	779	97.6	98	1633	91.4	91	1529	96.8
	K+k+	18	2.3	2	152	8.5	8.8	51	3.2
	K+k–	1	0.1	RARE	2	0.1	0.2	0	0.0
	Kp(a+b+)	14	2.3	RARE	29	2.2	2.3	18	1.3
	Kp(a–b+)	596	97.7	100	1322	97.9	97.7	1396	98.7
	Js(a+b+)	115	18.9	19	4	0.3	RARE	19	1.4
	Js(a+b–)	5	0.8	1	1	0.1	0	0	0.0
	Js(a–b+)	490	80.3	80	1339	99.6	100	1392	98.7
Duffy	Fy(a+b–)	142	17.8	9	350	19.6	17	571	36.1
	Fy(a+b+)	36	4.5	1	828	46.3	49	648	41.0
	Fy(a–b+)	165	20.7	22	604	33.8	34	350	22.1
	Fy(a–b–)	455	57.0	68	6	0.3	RARE	13	0.8
Kidd	Jk(a+b–)	424	53.3	51.1	450	25.2	26.3	380	24.0
	Jk(a+b+)	327	41.1	40.8	910	50.9	50.3	803	50.8
	Jk(a–b+)	45	5.7	8.1	429	24.0	23.4	398	25.2

CAUC = Caucasian; HISP = Hispanic.

(57%) and Jk(a–b+) (5.7%), as compared with published prevalence of 68.0 percent and 8.1 percent, respectively. The prevalence of the South Texas CAUC donor population for Kell, Duffy, and Kidd phenotypes compared with published reports. In the HISP population, the Fy(a+b–) phenotype was significantly higher at 36.1 percent, as compared with both the published prevalence for CAUC and black of 9 percent and 17 percent, respectively. There was no significant difference in the prevalence of Kell, Duffy, and Kidd phenotypes for the HISP donor as compared with both the published CAUC and black phenotypes.

Table 4 compares the prevalence of MNS blood group antigens in black and CAUC published phenotypes with that of black, CAUC, and HISP South Texas donors.[8] The prevalence of MNS phenotypes in the black population was comparable with the published prevalence, except for an increase in

Table 4. Prevalence of MNS blood group phenotypes: comparison of South Texas donors with published report[8]

		Black			CAUC			HISP	
		South Texas donors		Published reports	South Texas donors		Published reports	South Texas donors	
Blood group system	Phenotype	*N*	Prevalence (%)	Prevalence (%)	*N*	Prevalence (%)	Prevalence (%)	*N*	Prevalence (%)
MNS	M+N+S+s+	95	12.2	13	418	23.5	24	338	21.4
	M+N+S+s–	24	3.1	2	55	3.1	4	69	4.4
	M+N+S–s+	247	31.6	33	396	22.3	22	331	21.0
	M+N+S–s–	5	0.6	0.4	0	0.0	0	0	0.0
	M+N–S+s–	19	2.4	2	101	5.7	6	126	8.0
	M+N–S+s+	41	5.3	7	271	15.2	14	311	19.7
	M+N–S–s+	151	19.3	16	173	9.7	8	214	13.6
	M+N–S–s–	2	0.3	0.4	0	0.0	0	0	0.0
	M–N+S–s+	158	20.2	19	277	15.6	15	125	7.9
	M–N+S–s–	1	0.1	0.7	0	0.0	0	0	0.0
	M–N+S+s+	32	4.1	5	78	4.4	6	57	3.6
	M–N+S+s–	6	0.8	2	10	0.6	1	8	0.5

CAUC = Caucasian; HISP = Hispanic.

Table 5. Prevalence of Colton, Diego, Dombrock, Lutheran, Landsteiner-Wiener, and Scianna blood group phenotypes: comparison of South Texas donors with published reports[8]

		Black			CAUC			HISP	
		South Texas donors		Published reports	South Texas donors		Published reports	South Texas donors	
Blood group system	Phenotype	*N*	Prevalence (%)	Prevalence (%)	*N*	Prevalence (%)	Prevalence (%)	*N*	Prevalence (%)
Colton	Co(a+b+)	26	3.3	9.5*	123	6.9	9.5*	45	2.9
	Co(a+b–)	770	96.6	90*	1666	93.1	90*	1535	97.1
	Co(a–b+)	1	0.1	0.5*	1	0.1	0.5*	1	0.1
Diego	Di(a+b+)	2	0.3	<0.1	7	0.4	<0.1	98	6.2
	Di(a+b–)	1	0.1	<0.01	0	0.0	<0.01	4	0.3
	Di(a–b+)	785	99.6	>99.9	1765	99.6	>99.9	1473	93.5
Dombrock	Do(a+b+) Hy+ Jo(a+)	318	40.3	44	856	48.1	49	727	46.4
	Do(a+b+) Hy+ Jo(a–)	4	0.5	RARE	0	0.0	None	0	0.0
	Do(a+b–) Hy+ Jo(a+)	63	8.0	11	270	15.2	18	227	14.5
	Do(a+b–) Hy+ Jo(a–)	3	0.4	RARE	0	0.0	None	0	0.0
	Do(a–b+) Hy+ Jo(a+)	402	50.7	45	654	36.7	33	613	39.1
	Do(a–b+) Hy– Jo(a–)	1	0.1	RARE	0	0.0	None	0	0.0
Lutheran	Lu(a+b+)	37	4.6	7.4†	101	5.6	7.4†	42	2.7
	Lu(a+b–)	0	0.0	0.2†	3	0.2	0.2†	0	0.0
	Lu(a–b+)	761	95.4	92.4†	1687	94.2	92.4†	1540	97.4
Landsteiner-Wiener	LW(a+b+)	1	0.1	3†	9	0.5	3†	4	0.3
	LW(a+b–)	787	99.9	97†	1781	99.4	97†	1578	99.8
	LW(a–b+)	0	0.0	RARE†	1	0.1	RARE†	0	0.0
Scianna	SC:1,2	1	0.1	1	5	0.3	0	1	0.1
	SC:1,–2	792	99.9	99	1782	99.7	100	1581	99.9

CAUC = Caucasian; HISP = Hispanic.

*All populations.

†Most populations.

the M+N–S–s+ phenotype prevalence of 19.3 percent, as compared with the published 16.0 percent. The prevalence of MNS phenotypes in the South Texas CAUC donor population was comparable with that of published reports. The prevalence for the M+N–S+s+ phenotype in the HISP population was 19.7 percent, as compared with published CAUC and black phenotypes of 14.0 percent and 7.0 percent, respectively. In addition, the prevalence of the phenotype M–N+S–s+ in the HISP population was 7.9 percent, as compared with CAUC and black phenotypes of 15.0 percent and 19.0 percent, respectively.

Table 5 includes those blood group systems that contain high- and low-prevalence antigens. The prevalence of the Colton blood group system phenotype Co(a+b+) was 3.3 percent in the black population, 2.9 percent in the HISP population, and 6.9 percent in the CAUC population, as compared with the published reports of 9.5 percent in all populations in the U.S.[8] Within the Diego blood group system, the phenotypes of Di(a+b+) and Di(a+b–) for the HISP population had a prevalence of 6.2 percent and 0.3 percent, as compared with the published CAUC and black reports of less than 0.1 percent and less than 0.01 percent, respectively. Within the Lutheran blood group system, the phenotype Lu(a–b+) for the HISP population had a prevalence of 97.4 percent compared with the published report of 92.4 percent, yet there was a decrease of the Lu(a+b+) phenotype (2.7%) compared with the published (7.4%). Within the black population, the Dombrock blood group system phenotype combination of Do(a+b–)Hy+Jo(a+) was 8.0 percent, Do(a+b+)Hy+Jo(a+) was 40.3 percent, and Do(a–b+)Hy+Jo(a+) was 50.7 percent as compared with published reports of 11 percent, 44 percent, and 45 percent, respectively. The South Texas CAUC population phenotype prevalence was comparable with the published reports of the same ethnicity for those phenotypes (as seen in Table 5).

In Table 6, the antigen prevalence predicted by RBC genotyping is compared among black, CAUC, and HISP

Table 6. Hardy–Weinberg equilibrium two-allele frequency calculations in the South Texas donors

		Black			CAUC			HISP		
Kell	Phenotype*	K+k–	K+k+	K–k+	K+k–	K+k+	K–k+	K+k–	K+k+	K–k+
	H-W freq	0.02	2.40	97.51	0.19	8.35	91.46	0.03	3.18	96.80
	Frequency†	K = 1.25, k = 98.75			K = 4.36, k = 95.64			K = 1.61, k = 98.39		
	Phenotype*	Js(a+b–)	Js(a+b+)	Js(a–b+)	Js(a+b–)	Js(a+b+)	Js(a–b+)	Js(a+b–)	Js(a+b+)	Js(a–b+)
	H-W freq	1.05	18.39	80.56	0.00	0.45	99.55	0.00	1.34	98.66
	Frequency†	Js^a = 10.25, Js^b = 89.75			Js^a = 0.22, Js^b = 99.78			Js^a = 0.67, Js^b = 99.33		
	Phenotype*	Kp(a+b–)	Kp(a+b+)	Kp(a–b+)	Kp(a+b–)	Kp(a+b+)	Kp(a–b+)	Kp(a+b–)	Kp(a+b+)	Kp(a–b+)
	H-W freq	0.01	2.27	97.72	0.01	2.12	97.86	0.00	1.2	98.7
	Frequency†	Kp^a = 1.15, Kp^b = 98.85			Kp^a = 1.07, Kp^b = 98.93			Kp^a = 0.64, Kp^b = 99.3		
Colton	Phenotype*	Co(a+b–)	Co(a+b+)	Co(a–b+)	Co(a+b–)	Co(a+b+)	Co(a–b+)	Co(a+b–)	Co(a+b+)	Co(a–b+)
	H-W freq	96.52	3.45	0.03	93.14	6.74	0.12	97.05	2.93	0.02
	Frequency†	Co^a = 98.24, Co^b = 1.76			Co^a = 96.51, Co^b = 3.49			Co^a = 98.51, Co^b = 1.49		
Landsteiner-Wiener	Phenotype*	LW(a+b–)	LW(a+b+)	LW(a–b+)	LW(a+b–)	LW(a+b+)	LW(a–b+)	LW(a+b–)	LW(a+b+)	LW(a–b+)
	H-W freq	99.80	0.13	0.00	99.39	0.61	0.00	99.75	0.25	0.00
	Frequency†	LW^a = 99.94, LW^b = 0.06			LW^a = 99.6, LW^b = 0.31			LW^a = 99.87, LW^b = 0.13		
Kidd	Phenotype*	Jk(a+b–)	Jk(a+b+)	Jk(a–b+)	Jk(a+b–)	Jk(a+b+)	Jk(a–b+)	Jk(a+b–)	Jk(a+b+)	Jk(a–b+)
	H-W freq	54.47	38.66	6.86	25.59	49.99	24.42	24.43	49.99	25.57
	Frequency†	Jk^a = 73.81, Jk^b = 26.19			Jk^a = 50.59, Jk^b = 49.41			Jk^a = 49.43, Jk^b = 50.57		
Diego	Phenotype*	Di(a+b–)	Di(a+b+)	Di(a–b+)	Di(a+b–)	Di(a+b+)	Di(a–b+)	Di(a+b–)	Di(a+b+)	Di(a–b+)
	H-W freq	0.00	0.51	99.49	0.00	0.39	99.01	0.11	6.50	93.38
	Frequency†	Di^a = 0.25, Di^b = 99.75			Di^a = 0.2, Di^b = 99.8			Di^a = 3.37, Di^b = 96.63		
Lutheran	Phenotype*	Lu(a+b–)	Lu(a+b+)	Lu(a–b+)	Lu(a+b–)	Lu(a+b+)	Lu(a–b+)	Lu(a+b–)	Lu(a+b+)	Lu(a–b+)
	H-W freq	0.05	4.53	95.42	0.09	5.80	94.11	0.02	2.62	97.36
	Frequency†	Lu^a = 2.32, Lu^b = 97.68			Lu^a = 2.99, Lu^b = 97.01			Lu^a = 1.33, Lu^b = 98.67		

CAUC = Caucasian; HISP = Hispanic; H-W = Hardy–Weinberg; freq = frequency.

*Genotype-predicted antigen phenotype.

†Frequency of genotype-predicted antigen phenotype.

populations of South Texas donors based on the Hardy-Weinberg equilibrium. As would be expected, for the Kell blood group system, the prevalence of K in the CAUC population (4.3%) was higher than that in the black (1.3%) or HISP (1.6%) populations. There was a significant increase (10.3%) in the predicted prevalence of Js^a in the black population as compared with 0.22 percent in the CAUC and 0.67 percent in the HISP populations. In the Colton blood group system, there was an increased predicted prevalence of Co^b (3.5%) in the CAUC population, whereas predicted prevalence of only 1.8 percent and 1.5 percent were observed with the black and HISP populations, respectively. In the Kidd blood group system, differences in prevalence were evident with Jk^a at 73.8 percent for black, but only 50.9 percent and 49.4 percent for CAUC and HISP, respectively. There was a significant increase in prevalence of Di^a at 3.4 percent in the HISP population as compared with 0.3 percent in the black and 0.2 percent in the CAUC populations.

Discussion

RBC transfusions can save a patient's life; however, this life-saving component can also have adverse effects in the patient. For example, it can cause shortened RBC survival, leading to the increased need for blood transfusion. This step may cause iron overload in selected individuals.[9] Transfusions can cause DHTR, hyperhemolysis syndrome, episodes of pain, acute chest syndrome, acute renal failure, chronic positive direct antiglobulin test, and development of warm autoantibodies.[10] Patients who are transfused with more than 10 units of RBCs have a higher rate of becoming alloimmunized than those who are transfused with fewer than 10 units.[11,12] The rate of alloimmunization is as high as 43 percent in patients with SCD, with antibodies to antigens in the Rh and Kell blood group systems being the most frequently identified.[9,13] Antibodies to C and E are identified over two-thirds of the time.[10] Moreover, the U.S. Food and Drug Administration reported five transfusion-related fatalities in the category of

HTR (non-ABO) for fiscal year 2013.[14] These included the following antibody specificities: anti-c, anti-E, anti-Jk^a, anti-Jk^b, and anti-K.

It has been documented that providing phenotypically matched blood drastically decreases the alloimmunization rate.[15] One study showed dramatic decreases of alloimmunization—from 35 percent to 0 percent—in patients with SCD who received extended phenotype-matched blood (Rh, Kell, MNS, Duffy, and Kidd blood group systems). A second study showed a decrease from 34 percent to 7 percent.[16] Another study provided blood from donors ethnically similar to the recipients; this was based on antigen prevalence within black and Caucasian populations. Results showed a higher probability of finding an extended phenotype-matched donor for a patient with SCD in the black donor population (93%) than in the Caucasian donor population (7%).[10,17] In the black population, many RH alleles encoding for many complex phenotype variants have been described; this may explain why one cohort study demonstrated that using limited phenotype matching did not show a decrease in alloimmunization rate with Rh antibodies in this population.[16] However, providing blood that is genotypically matched instead of serologically phenotyped for the Rh blood system has been found to further decrease alloimmunization rates.[5,10,18]

The lack of standardization in providing limited and/or extended phenotype-matched donor units among transfusion services is attributed to pressures of cost management of transfusion therapy for SCD.[19] One cohort study compared the cost of antigen-matching strategies for (1) matching only those patients with SCD who have developed or have a history of antibodies and (2) prospective matching regardless of antibody development.[13] To provide limited or extended matching, mass screening of blood donors using genotyping methods would need to be performed on an ongoing basis. Donor genotyping can not only increase antigen-negative inventory, but can also identify rare donors who lack high-prevalence antigens. Furthermore, the use of other RH DNA analysis testing kits can manage RH typing variations, but will not resolve ABO discrepancies or find weak D that would otherwise not be identified by conventional serologic screening.[20–22] There are some limitations of genotyping—for example, not being able to accurately predict donors with less common silencing mutations, causing the phenotype to be predicted as expressed, thus a false-positive for the antigen; the most common silencing mutation available in most commercial RBC genotyping panels is the FY GATA mutation.[22–24] In addition, DNA testing turnaround time takes hours, not all the alleles are known for each ethnic group, the cost between genotyping and serologic phenotyping varies, and genotype and serologic results may not agree.[22–24]

In conclusion, this is the first study to determine the prevalence of various RBC phenotypes among the South Texas blood donor population using a genotyping methodology. There is limited availability of published data for blood group phenotype prevalence for Hispanics; therefore, this study can establish a benchmark. This valuable information provides antigen-negative prevalence within the three major ethnic groups (black, CAUC, HISP) of South Texas blood donors. Because frequently transfused patients have higher probability of developing antibodies, knowledge of antigen prevalence in different ethnicities can assist in complex antibody identification cases and can help determine the most appropriate antigen-matched blood product to provide. Given that alloimmunization occurs in up to 43 percent of patients with SCD, providing limited and/or extended matching to all may be a challenge in the South Texas population. Creating effective algorithms to genotype black, CAUS, and HISP blood donors can potentially increase the rare donor database. This step can supply adequate antigen-negative blood to the unique diversity of South Texas patients, possibly preventing alloimmunization and supporting those patients who are already alloimmunized.

Based on the data collected from South Texas donors, our donor center will select groups A and O donors who are black, instead of the current practice of randomly selecting black donors for further genotyping. Black donors have a higher probability of phenotyping as R_0r, Fy(a–b–), and Jk(a+b–). Selecting black donors will decrease alloimmunization in our patients with sickle cell disease as well as ensure an adequate supply for patients of this ethnicity who develop alloantibodies, thus decreasing the delay in finding compatible blood. Also, specifically selecting Hispanic donors will increase the R_1R_1, R_2R_2, Fy(a+b–), and Jk(a–b+) rare donor inventory, providing adequate rare blood to HISP, black, and CAUC populations. In addition, there is a higher probability in finding rare blood that is Di(a+b–), given that the prevalence of Di(b+) donors is 96.6 percent in Hispanics. Alloanti-Di^b is clinically significant, and is known to cause mild to delayed transfusion reactions. Using this algorithm to genotype South Texas donor populations should start to establish an adequate rare donor pool to supply rare blood to this diverse population. This step also challenges other Texas and diverse geographically located donor centers to publish their phenotype prevalences and establish appropriate algorithms to maintain adequate rare blood supply.

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